BACAMPICILLIN IN THERAPY OF LOWER RESPIRATORY INFECTIONS*

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BACAMPICILLIN is a prodrug which, after oral administration, hydrolyzes rapidly to ampicillin[1] and apparently completely converts to the parent drug because even the most sensitive techniques have failed to demonstrate bacampicillin in the serum.[2] Because of its rapid absorption and conversion, a high level of the drug is quickly available in blood and tissues.

Successful treatment of lower respiratory tract infections requires ample and readily available antimicrobial concentrations at the infection site. Bacampicillin can provide this,[3] and the drug can be given orally in twice daily doses, thereby enhancing patient compliance. A study was designed to test the efficacy of bacampicillin in patients with serious lower respiratory tract infections.

LOWER RESPIRATORY TRACT INFECTIONS

Patients. Fifteen patients, ranging in age from 17 to 76 years, with clinical and/or radiologic evidence of pneumonia and/or acute bronchitis were included in the study. There were 11 men and four women. Table I shows these data and the diagnoses.

Excluded were patients who were pregnant, had known or suspected allergies to penicillins or cephalosporins, had hepatic disease, had impaired renal function, required other concomitant antimicrobial therapy or had received such therapy during the past month, had infectious mononucleosis, had impaired immunologic function, or had chronic lower respiratory tract infections.

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TABLE I. DIAGNOSIS OF PATIENTS WITH LOWER RESPIRATORY TRACT INFECTION

Age	*Sex*	*Diagnosis*
76	M	Right lower lobe pneumonia
22	F	Right middle lobe pneumonia
55	M	Left lower lobe pneumonia
55	M	Right lower lobe pneumonia
27	M	Right lower lobe & left upper lobe pneumonia
17	M	Left lower lobe pneumonia
25	M	Right upper lobe & left lower lobe pneumonia
35	M	Right middle lobe pneumonia
34	M	Right middle lobe pneumonia
20	F	Left lower lobe pneumonia
75	M	Right lower lobe pneumonia
55	M	Bronchitis
54	F	Bronchitis
45	M	Bronchitis
52	F	Bronchitis

Diagnosis. The clinical or radiologic diagnosis was confirmed by bacteriologic culture. The culture material (sputum, blood) was collected before treatment began. Entry into the study required the presence of one of the following pathogens in the sputum: *Streptococcus pneumoniae* (pneumococcus), *Streptococcus pyogenes*, or *Hemophilus influenzae*.

Dosage. The patients were given two 400 mg bacampicillin tablets every 12 hours for 10 days.

Patient evaluation. The efficacy of the drug was evaluated on the basis of microbiologic, clinical, laboratory, and radiologic results (Table II). Patients were evaluated clinically before treatment began, 48 to 72 hours after the start of therapy, on day 10 of therapy (the last day), and one week after therapy. They were examined for the following signs and symptoms: cough, fever, sputum production and purulence, rales, rhonchi, or wheezes on auscultation of the lung fields, dyspnea, chest pain or discomfort, and chills.

Specimens (expectorated sputum) for culture and susceptibility testing were obtained before treatment, 48 to 72 hours after initiation of therapy, and on day 10. In addition, blood cultures were obtained prior to therapy. The sputum specimens were cultured aerobically. Blood was cultured both aerobically and anaerobically. Bacterial isolates were tested for antibiotic susceptibility by the Kirby-Bauer disk diffusion technique.

Each patient had routine laboratory tests performed prior to the initiation of therapy and on day 10. These tests included: complete blood

TABLE II. EVALUATION OF PATIENTS WITH LOWER RESPIRATORY TRACT INFECTION

Clinical evaluation (before Rx, 48–72 hours after Rx starts, day 10, one week later)
- Cough
- Fever
- Sputum production and purulence
- Rales, rhonchi, and/or wheezing on auscultation
- Dyspnea
- Chest pain or discomfort
- Chills

Microbiologic evaluation
- Blood culture (before Rx)
  - Aerobically
  - Anaerobically
- Sputum culture (before Rx, 48–72 hours, day 10)
  - Aerobically
  - Anaerobically
- Antibiotic susceptibility of bacterial isolates
  - Disk diffusion technique (Kirby-Bauer)

Laboratory evaluation (before treatment and on day 10)
- Complete blood count with differential leukocyte count
- Serum bilirubin
- Serum alkaline phosphatase
- Serum SGOT
- Serum SGPT
- Serum creatinine or blood ureanitrogen
- Urinalysis

Radiologic evaluation (before treatment and on day 10 or earlier)
- Posteroanterior chest roentgenograms
- Lateral chest roentgenograms

count with differential leukocyte count, serum, bilirubin, alkaline phosphatase, SGOT, SGPT, creatinine, BUN, and urinalysis. Prior to starting therapy, each patient also underwent radiologic study. Posteroanterior and lateral chest roentgenograms were obtained and were repeated on day 10. The purpose of the study was described to each patient, and each signed an informed consent form.

Results. In three of the 15 patients, no organism could be demonstrated microbiologically in the pretreatment cultures. These patients were followed because they had clinical or radiologic evidence, respectively, of right lower lobe pneumonia or bronchitis.

Pathogens identified in 12 of the 15 patients were pneumococcus of various types (nine patients) and *Hemophilus influenzae* (three patients) (Table III). Nine of the 10 patients with bacteriologically demonstrated pnuemonia had a pneumococcal infection, the 10th patient had a *H.*

TABLE III. ORGANISMS CULTURED FROM PATIENTS WITH LOWER RESPIRATORY TRACT INFECTION

Organism	*No. of patients*
Pneumonia patients	
Hemophilus influenzae	1
Pneumococcus	
Type 4	1
Type 9	1
Type 14	1
Type 16	2
Type 18	1
Type 19	2
Type 28	1
None	1
Bronchitis patients	
Hemophilus influenzae	2
None	2

influenzae infection. No bacterial pathogen was identified in the eleventh pneumonia patient. Both patients with bacteriologically demonstrated bronchitis had *Hemophilus influenzae* infections.

Cultures revealed that pathogens were eliminated in all the 12 patients by day six (Table IV). Of the 10 patients with bacterial pneumonia, cultures became negative in one day in three patients, in two days in four, and in three days in three. Of the two patients with bronchitis, the cultures were negative in five and six days, respectively.

Roentgenograms were obtained in 13 of the 15 patients. Generally, the films were obtained on day 10. However, in some cases clinical improvement indicated that roentgenograms might be clear earlier. When the films were done, they indeed showed a complete clearing at seven days in the pneumonia patient (Table IV). Seven patients (all with pneumonia) had no infiltrates at 10 days. One patient showed only some clearing at 10 days but was clinically well; one alcoholic patient had a residual infiltrate at 10 days; and one had almost clear lungs at 10 days. Two patients were not evaluated radiologically; both had acute bronchitis, but neither of these patients had a pathogenic organism on culture (Table V).

Each of the 15 patients, including those without demonstrable organisms in the sputum, responded to the bacampicillin treatment. Microbiologically, pathogens were eliminated by day six in the 12 patients with positive cultures. Of the 13 of the 15 who had radiologic studies, clearing or partial clearing was observed by day 10 (Table VI).

TABLE IV. RESULTS OF THERAPY IN PATIENTS WITH LOWER RESPIRATORY TRACT INFECTION

*Diagnosis**	*Organism***	*Days to eradicate in culture*	*Radiologic response*
RRL pneumonia	None	—	Clear, 10 days
RML pneumonia	Pneu T18	2	Clear, 10 days
LLL pneumonia	Pneu T28	1	Clear, 7 days
RLL pneumonia	Pneu T16	1	Some clearing, 10 days (clinically clear)
RRL & LUL pneumonia	Pneu T4	1	Clear, 10 days
LLL pneumonia	Pneu T16	3	Clear, 10 days
RUL & LLL pneumonia	Pneu T9	2	Clear, 10 days
RML pneumonia	Pneu T14	2	Partially clear, 10 days
RML pneumonia	Pneu T19	2	Clear, 10 days
LLL pneumonia	Pneu T19	3	Clear, 10 days
RLL pneumonia	*H. influenzae*	3	Almost clear, 10 days
Bronchitis	None	—	Clear clinically Roentgenogram not done
Bronchitis	None	—	?
Bronchitis	*H. influenzae*	5	Clear, 7 days
Bronchitis	*H. influenzae*	6†	Clear, 5-6 days

*RLL = right lower lobe, RML = right middle lobe, LLL = left lower lobe, LUL = left upper lobe, RUL = right upper lobe.
**Pneu T = pneumococcus type.
†A culture was done on day 2, but the organisms were still present at that time.

TABLE V. CULTURE CLEAR RATE (12 PATIENTS)

	Day 1	*Day 3*	*Day 4*	*Day 5*	*Day 6*
Pneumonia (9 *S. pneumoniae*, 1 *H. influenzae*)					
No. of patients	3	4	3		
Percentage	30	40	30		
Cumulative percentage	30	70	100		
Bronchitis (H. influenzae)					
No. of patients				1	1
Percentage				50	50
Cumulative percentage				50	100

Two patients experienced side effects. These did not require treatment, nor was it necessary to discontinue the bacampicillin. One patient had mild nausea, and on being questioned she said that she had taken the dose on an empty stomach. Since bacampicillin tablets may be administered

TABLE VI. CULTURE CURE RATE (10 PNEUMONIA PATIENTS, 2 BRONCHITIS PATIENTS)

	Day 1	*Day 3*	*Day 4*	*Day 5*	*Day 6*
No. of patients	3	4	3	1	1
Percentage	25	33	25	9	8
Cumulative percentage	25	58	83	91	100

without regard to meals, subsequent doses were taken after food, and she had no further difficulties. The second patient complained of mild diarrhea for three days. There were no significant changes in the laboratory results.

DISCUSSION

The usual dosage of bacampicillin is 800 mg/day although 1600 mg/day may be used for severe infections or those caused by less susceptible organisms. Because certain pneumonias and acute bronchitis are considered severe infections and the patients included in this study were acutely ill, the higher dose of bacampicillin (1600 mg/day) was administered.

Bacampicillin had been given in this large a dose in a previous study.[3] The patients in this earlier study had pneumonia, exacerbations of chronic bronchitis, and bronchiectasis. The major pathogens were *Streptococcus pneumoniae, Hemophilus influenzae*, and β-hemolytic streptococcus. The high doses of bacampicillin in these 25 patients resulted in 21 clinical cures and four patients who reported improvement. Moreover, the pathogen disappeared from culture in all 25 of the patients, five of whom had had positive blood cultures.

The present study indicates that bacampicillin is effective in the treatment of serious lower respiratory infections, including pneumonia and bronchitis.

In this study, therapy was begun before receiving the results of the microbiologic culture, which is why three patients who had clinical evidence of a lower respiratory tract infection but who had no evidence of any organism on culture were treated. Had any pathogen proved to be resistant to ampicillin, the bacampicillin would of course have been discontinued and other treatment instituted. Because good results were obtained with bacampicillin, this was not necessary.

Because bacampicillin need be given only twice a day, the regimen is convenient for treating outpatients and may enhance patient compliance. Even in the hospital setting, convenience is a factor because twice daily doses relieve the nursing staff from an additional round of the drug.[3] Consequently, savings based upon reduced nursing and pharmacist labor costs could be realized by hospitals utilizing medications that require fewer daily doses.

Among the patients with lower respiratory tract infections were two alcoholics, one diabetic, and one patient with asthma. Bacampicillin proved equally effective in these compromised situations.

Conclusion

Bacampicillin was effective in the treatment of serious lower respiratory tract infections. It is easily administered in twice daily doses. In two of the 15 patients it produced minor gastrointestinal side effects, but these were not sufficiently disabling or significant to stop administration of the drug.

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